‘Heroin on trial’: Heroin-Assisted Treatment - Overview of the RIOTT trial and its findings

Professor Sir John Strang
National Addiction Centre, King’s College London, UK
Thanks (personal & institutional)

- Special thanks to the many patient/participants, clinical and policy colleagues, research colleagues
- Wider international community of interest and commitment to science
- EMCDDA - commissioning ‘Insights’ Monograph (and supply of complimentary copies)
Declarations (personal & institutional)

- NHS provider (community & in-patient); also Phoenix House, Lifeline, Clouds House, KCA (Kent Council on Addictions).
- Dept of Health, NTA, Home Office, NACD, EMCDDA, WHO, UNODC, NIDA.
- Dialogue and work with pharmaceutical companies re actual or potential development of new medicines for use in the addiction treatment field (including (past 3 years) Martindale, Indivior, MundiPharma, Braeburn/Camurus and trial product supply from iGen and Camurus.
- SSA (Society for the Study of Addiction); UKDPC (UK Drug Policy Commission), and two Masters degrees (taught MSc and IPAS) and an Addictions MOOC.
- Work also with several charities (and received support) including Action on Addiction, and also with J Paul Getty Charitable Trust (JPGT) and Pilgrim Trust.
- The university (King’s College London) has registered intellectual property on a buccal naloxone formulation, and JS has been named in a patent registration by a Pharma company as inventor of a novel concentrated naloxone nasal spray.
- JS and other speakers have contributed to local, national and international guidelines on treatments; speaking today in individual capacities.
To complement the development of existing services, heroin should be available on prescription to all those who have a clinical need for it.

The number of people receiving heroin will increase as overall numbers in treatment grow.

The administration of prescribed heroin for those with a clinical need will take place in safe, medically supervised areas with clean needles. Strict and verifiable measures will be in place to ensure there is no risk of seepage into the wider community.

*UK Government Drug Strategy, 2002*
Target population

Entrenched heroin addicts who have repeatedly been found to fail to benefit from existing treatments

(despite treatment, continuing to inject heroin on all/most days per month)
RIOTT trial randomisation

Injecting heroin User in opioid Maintenance Treatment for 6 months

Diamorphine IV/IM +/- oral methadone

Methadone Ampoules IV/IM +/- oral methadone

Enhanced Oral Methadone
Primary outcome

Retention in treatment  X

Reducing/quititng ‘street heroin’

Other drug use; well-being;

Criminal behaviour  ?

Wider recovery
Primary outcome measure

<table>
<thead>
<tr>
<th>Primary outcome</th>
<th>Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduction in street heroin use</td>
<td>The proportion of subjects in each group who cease regular street heroin use</td>
</tr>
</tbody>
</table>
'responder' or 'abstinent'?

Major reduction in frequency of use of 'street heroin'

Completely abstinent from 'street heroin'
Which measure of primary outcome?

- Urine test results
- Observations and measurements
- Self-report
Validation of techniques to detect illicit heroin use in patients prescribed pharmaceutical heroin for the management of opioid dependence

S. Paterson¹, N. Lintzeris²,3, T. B. Mitchell², R. Cordero¹, L. Nestor² & J. Strang²

Toxicology Unit, Imperial College London, UK¹ and National Addiction Centre, Institute of Psychiatry, Kings College London, South London and Maudsley Trust, UK² and National Drug and Alcohol Research Centre, University of New South Wales, Australia³

Correspondence to:
Nicholas Lintzeris
c/o National Addiction Centre
PO Box 48
4 Windsor Walk
Denmark Hill
London SE5 8AF
UK
E-mail: n.lintzeris@iop.kcl.ac.uk

Submitted 5 November 2004; initial review completed 31 March 2005; final version accepted 9 May 2005

ABSTRACT

Background The clinical implementation and evaluation of heroin substitution programmes have been confounded by the lack of objective and validated biomarkers for illicit heroin use in patients prescribed pharmaceutical heroin. This study examined the capacity to detect illicit heroin use by gas chromatography–mass spectrometry (GC-MS) analysis of urine samples for the presence of opium impurities common to illicit, but not pharmaceutical heroin.

Aims To characterize the diagnostic properties of the metabolites of noscapine and papaverine in comparison to morphine as a gold-standard marker of illicit heroin use; and to examine the relationships between the self-reported time since most recent heroin use and the detection of these opioids in urine.
Metabolism of “illicit” Heroin

Diamorphine → Morphine

Diamorphine → Noscapine → 6-Demethylmeconine

Diamorphine → Papaverine → 4,6-Dihydroxypapaverine

Codeine → 6-Monoacetyl morphine

Meconine

6-Hydroxypapaverine
Supervised injectable heroin or injectable methadone versus optimised oral methadone as treatment for chronic heroin addicts in England after persistent failure in orthodox treatment (RIOTT): a randomised trial

John Strang, Nicola Metrebian, Nicholas Lintzeris, Laura Potts, Tom Carnwath, Soraya Mayet, Hugh Williams, Deborah Zador, Richard Evers, Teodora Groshkova, Vikki Charles, Anthea Martin, Luciana Forzisi

Summary

Background Some heroin addicts persistently fail to benefit from conventional treatments. We aimed to compare the effectiveness of supervised injectable treatment with medicinal heroin (diamorphine or diacetylmorphine) or supervised injectable methadone versus optimised oral methadone for chronic heroin addiction.

Methods In this multisite, open-label, randomised controlled trial, we enrolled chronic heroin addicts who were receiving conventional oral treatment (≥6 months), but continued to inject street heroin regularly (≥50% of days in preceding 3 months). Randomisation by minimisation was used to assign patients to receive supervised injectable methadone, supervised injectable heroin, or optimised oral methadone. Treatment was provided for 26 weeks in three supervised injecting clinics in England. Primary outcome was 50% or more of negative specimens for street heroin on weekly urinalysis during weeks 14–26. Primary analysis was by intention to treat; data were adjusted for centre, regular crack use at baseline, and treatment with optimised oral methadone at baseline. Percentages were calculated with Rubin’s rules and were then used to estimate numbers of patients in the multiple imputed samples. This study is registered, ISRCTN01338071.

Findings Of 301 patients screened, 127 were enrolled and randomly allocated to receive injectable methadone (n=42 patients), injectable heroin (n=43), or oral methadone (n=42); all patients were included in the primary analysis. At 26 weeks, 80% (n=101) patients remained in assigned treatment: 81% (n=34) on injectable methadone, 88% (n=38) on injectable heroin, and 69% (n=29) on oral methadone. Patients on injectable heroin were significantly more likely to have achieved the primary outcome (72% [n=31]) than were those on oral methadone (27% [n=11], OR
Findings - to begin at the end

Four important conclusions, as I see them

• SIH (heroin) group strongest achievement

• SIM (inj methadone) better than OOM group

• OOM (optimised oral) – still show benefit

• Rapid onset of benefit and gain
Results

Figure 1 shows the trial profile. Patients were recruited between September, 2005, and August, 2008, and

Figure 4: Proportion of responders* at weeks 14–26
Error bars are 95% CIs. Analysis adjusted for centre, regular crack use at baseline, and treatment with optimised oral methadone at baseline. *50% or more of urine samples negative for street heroin during weeks 14–26.
**Figure 5**: Proportion of participants who were abstinent* from street heroin at weeks 23–26

Error bars are 95% CIs. Analysis adjusted for centre, regular crack use at baseline, and treatment with optimised oral methadone at baseline. *Negative results in all four samples taken in weeks 23–26.
RIOTT - data on ‘responders’ and ‘non-responders’ – broken down as % - at baseline (OOM, SIM, SIH)

RIOTT treatment group

non-responder

responder

OOM SIM SIH

RIOTT data on ‘responders’ and ‘non-responders’ – broken down as % - at baseline (OOM, SIM, SIH)
RIOTT - data on ‘responders’ and ‘non-responders’ – broken down as % - at Months 4-6 (OOM, SIM, SIH)
RIOTT - data on ‘responders’ and ‘non-responders’ – broken down as % - at Months 4-6 (OOM, SIM, SIH)
RIOTT - data on ‘responders’ and ‘non-responders’ – broken down as % - at Months 4-6 (OOM, SIM, SIH)
RIOTT - data on ‘responders’ and ‘non-responders’ – broken down as % - at Months 4-6 (OOM, SIM, SIH)
Figure 6: Proportion of participants abstinent from street heroin per week by data for urine drug screen (intention-to-treat sample)
Percentage of participants not using illicit heroin by week (ITT sample)
Percentage of participants not using illicit heroin by week (ITT sample)
Percentage of participants not using illicit heroin by week (ITT sample)
New heroin-assisted treatment

Recent evidence and current practices of supervised injectable heroin treatment in Europe and beyond

Authors
John Strang, Teodora Groshkova and Nicola Metrebian
Drugs: protecting families and communities

The 2008 drug strategy

First Edition
“... rolling out the prescription of injectable heroin and methadone to clients who do not respond to other forms of treatment, subject to the findings, due in 2009, of pilots exploring the use of this type of treatment”.

(H.M.Government Drug Strategy, 2008)
News story

Invitation to Tender: the piloting of supervised injectable Opioid Treatment

Organisation: Department of Health
Page history: Published 1 March 2012

The DH is looking to contract with Service Providers to develop a cost-effective model of delivering a high intensity treatment intervention...

The DH is looking to contract with Service Providers to develop a cost-effective model of delivering a high intensity treatment intervention to a thinly spread population, with a view to demonstrating how IOT can be appropriately commissioned in the future. The nature of the service to be delivered requires hours of opening which enable twice daily supervised injecting, 7 days per week.

The proposed programme will explore how to maximise the cost-effectiveness of IOT to secure future commissioning arrangements:

1. We intend to award between two and six contracts, on the basis of open competition, with lots closing until 31 March 2015.
Thank you